

Inventors: Seidman and Théorêt  
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(a) administering a 6-mercaptopurine drug to a subject having said immune-mediated gastrointestinal disorder; and

(b) determining a level of a 6-mercaptopurine metabolite in said subject having said immune-mediated gastrointestinal disorder,

wherein a level of said 6-mercaptopurine metabolite less than a predetermined minimal therapeutic level indicates a need to increase the amount of 6-mercaptopurine drug subsequently administered to said subject, thereby increasing therapeutic efficacy, and

wherein a level of said 6-mercaptopurine metabolite greater than a predetermined toxic level of said 6-mercaptopurine metabolite indicates a need to decrease the amount of 6-mercaptopurine drug subsequently administered to said subject, thereby reducing toxicity associated with 6-mercaptopurine drug treatment of said immune-mediated gastrointestinal disorder.

26/ 36. (New) The method of claim 25, wherein said immune-mediated gastrointestinal disorder is IBD.

27/ 37. (New) The method of claim 26, wherein said subject having IBD is a pediatric subject.

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38. (New) The method of claim 25, wherein said immune-mediated gastrointestinal disorder is selected from the group consisting of lymphocytic colitis, microscopic colitis, collagenous colitis, autoimmune enteropathy, allergic gastrointestinal disease and eosinophilic gastrointestinal disease.

39. (New) The method of claim 35, wherein said 6-mercaptopurine metabolite is 6-thioguanine.

40. (New) The method of claim 39, wherein a predetermined minimal therapeutic level of 6-thioguanine is a level corresponding to about 230 pmol per  $8 \times 10^8$  red blood cells.

41. (New) The method of claim 39, wherein a predetermined toxic level of 6-thioguanine is a level corresponding to about 400 pmol per  $8 \times 10^8$  red blood cells.

42. (New) The method of claim 35, wherein said 6-mercaptopurine metabolite is 6-methyl-mercaptopurine.

43. (New) The method of claim 42, wherein a predetermined toxic level of 6-methyl-mercaptopurine is a level corresponding to about 7000 pmol per  $8 \times 10^8$  red blood cells.

44. (New) The method of claim 35, wherein said level of said 6-mercaptopurine metabolite is determined in red blood cells.

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<sup>30</sup>~~45~~. (New) The method of claim <sup>29</sup>~~44~~, wherein said level is determined using high pressure liquid chromatography.

<sup>31</sup>~~46~~. (New) The method of claim <sup>25</sup>~~35~~, wherein said toxicity associated with <sup>said</sup>~~6-mercaptopurine~~ drug treatment is selected from the group consisting of hepatic toxicity and hematologic toxicity.--

#### REMARKS

Claims 1 to 34 are pending in this application. New claims 35 to 46 have been added. Upon entry of the present amendment, claims 1 to 46 will be pending.

Applicants appreciate the courtesy extended by the Examiner in the telephone discussion with Applicants' representative on September 1, 1999.

For the Examiner's convenience, Applicants enclose a copy of Form 1449 that was filed with the Information Disclosure Statement mailed August 26, 1999. Applicants have not enclosed additional copies of these references but will be happy to do so upon the Examiner's request. Applicants also submit herewith a supplemental Information Disclosure Statement and Form 1449 containing additional references, along with copies of the new references.

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